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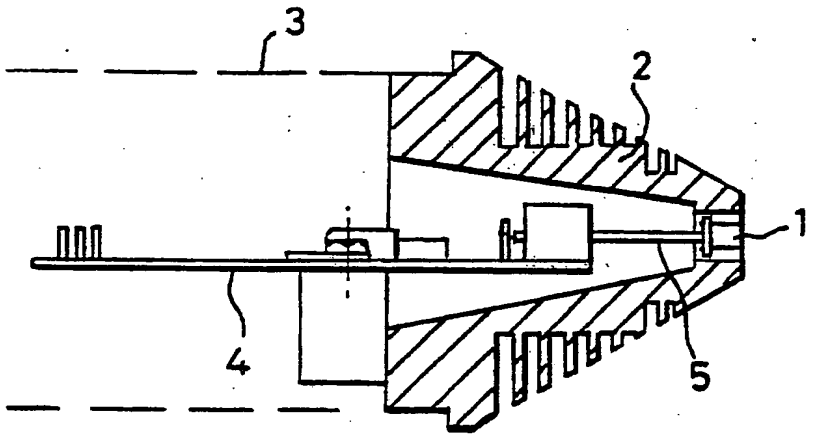
(54) Title: PROBE, AND METHOD OF USE THEREOF FOR BIOMUDULATION OF TISSUE, NERVE AND IMMUNE SYSTEMS



(57) Abstract

A probe (3) carries a semiconductor laser (1) for biomodulation of tissue, nerve and immune systems. To avoid losses due to radio frequency generation the driving electronics circuit is mounted on a printed circuit board (4) inside the probe. In operation discrete macropulses, each containing a series of micropulses, are generated.

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PROBE, AND METHOD OF USE THEREOF FOR BIOMODULATION OF TISSUE, NERVE AND IMMUNE SYSTEMS

This invention relates to probes, and methods of use thereof, for biomodultion of tissue, nerve and immune systems by frequency modulation of semiconductor lasers.

It has become apparent, through our recent research, that an important parameter for the observed laser biomodulation effect (stimulation or inhibition) is the method of delivering the visible or invisible light energy into the target material. We have also demonstrated that all other conditions being constant (e.g. wavelength, power density and energy density) the pulsing frequency and pulsing duration modulation of the laser light varies the biomodulation action.

It is, therefore, one object of the present invention, to provide a probe wherein the pulsing frequency and pulsing duration modulation can be very economically and efficiently controlled and applied.

According to the invention, there is provided a probe for the biomodulation of tissue, nerve and immune systems having a semiconductor laser mounted thereon for

delivering an electromagnetic beam to the area to be treated and electronic means so mounted within the probe closely adjacent the laser for stimulating the laser for the emission of a pulsating visible or invisible infared light constituting the said beam as thereby substantially to eliminate losses due to radio frequency and microwave generation. Very advantageously the electronic means is arranged to pulse the laser light with micropulses of nonosecond or picosecond duration and then modulate the light again by pulsing the laser with micropulses of millisecond, microsecond or nanosecond duration.

The invention also includes the method of effecting biomodulation (stimulation on inhibition) by delivering visible or invisible light energy into a target tissue, nerve or immune system by means of a probe as aforesaid.

In order that the invention may be clearly understood and readily carried into effect a probe and manner of operating such probe for biomodulation of tissue, nerve or an immune system will now be described, by way of example, with reference to the accompanying drawings, in which:-

Figure 1 is a diagrammatic sectional elevation of the probe,

Figure 2 is a circuit diagram comprising an electrical assembly in the probe, and

Figure 3 is an explanatory diagram.

Referring to Figure 1, the probe comprises a laser diode 1 for projecting a monochromatic beam in the visible or infrared range of the spectrum from the tip of a tapered and finned heat sink 2 terminating the probe 3. The laser diode 1 is driven and controlled through the medium of an electric circuit (Figure 2) carried by a printed circuit board 4 and connected to the laser diode 1 by a sleeved lead 5.

The circuit comprises oscillator frequency

control, beam oscillator, beam power control, beam power supply and beam control logic as described in Patent Application No. EP-A-0320080 and the circuit is arranged for the beam to be modulated periodically to operate as shown in Figure 3. Thus, in each duty period A there is a macroperiod B followed by an off time C. In each macroperiod B there is a series of similar microperiods D. The following table shows experimental results obtained with this form of operation with an output wavelength of 850 mm and a series of oscillator frequencies ranging from 2.5 Hz and 5KHz.

850	PROBE	PULSE	WIDTHS		
3ML FREQUENCY	DUTY PERIOD	CYCLE OFF-TIME	80% MACRO-PULSE	MICRO-PULSE	No.of MICRO PER MACRO
	A	C	B	D	
2.5Hz	400msec	80mSec	320mSec	350nSec	96.969
5Hz	200mSec	40mSec	160mSec	350nSec	48,484
10Hz	100mSec	20mSec	80mSec	350nSec	24,242
16Hz	62.5mSec	12.5mSec	50mSec	350nSec	15,151
20Hz	50mSec	10mSec	40mSec	350nSec	12,121
40Hz	25mSec	5mSec	20mSec	350nSec	6,060
80Hz	12.5mSec	2.5mSec	10mSec	350nSec	3,030
160Hz	6.25mSec	1.25mSec	5mSec	350nSec	1,515
292Hz	3.42mSec	684 Sec	2.74mSec	350nSec	830
700Hz	1.43mSec	286uSec	1.14mSec	350nSec	345
1KHz	1mSec	200uSec	800uSec	350nSec	242
5KHz	200 Sec	40uSec	160uSec	350nSec	48

By way of example, in one application of a system as described above the electromagnetic output laser beam has a wavelength of 850 mm and a frequency of 352.9×10^3 GHz pulsed at 300,000 Hz and additionally

modulated at a frequency of from 1 Hz to 2GHz. Above a pulsation frequency of 5000 Hz radio frequencies also arise and in order to avoid the losses due to transverse dispersion that these would involve if transmitted along a cable the printed circuit board 4 is located in the probe itself as shown in Figure 1.

In summary the invention enables the semiconductor laser light to be pulsed up to 3GHz with micropulses of nanosecond or picosecond duration and when modulated again with a carrier frequency by pulsing the diode with macropulses of millisecond, microsecond or nanosecond duration. The macropulses can be square or sinusoidal in shape whilst the micropulses are square. By incorporating the circuitry in the head of the probe interference from radio frequency (KHz, uHz) and microwave (GHz) generation is eliminated.

CLAIMS

1. A probe (3) for the biomodulation of tissue, nerve and immune systems characterised by a semiconductor laser (1) mounted thereon for delivering an electromagnetic beam to the area to be treated and electronic means (4, 5) so mounted within the probe (3) closely adjacent the laser (1) for stimulating the laser (1) for the emission of a pulsating visible or invisible infared light constituting the said beam as thereby substantially to eliminate losses due to radio frequency and microwave generation

2. A probe according to Claim 1, characterised in that the electronic means (4, 5) is arranged to pulse the laser (1) light with micropulses of nanosecond or picosecond duration and then modulate the light again by pulsing the laser (1) with micropulses of millisecond, microsecond or nanosecond duration.

3. A probe according to Claim 2, characterised in that it is arranged for the laser (1) light to be pulsed up to 3GHz.

4. A probe according to Claim 2 or Claim 3, characterised in that it is arranged for the macropulses to be square or sinusoidal in shape and the micropulses to be square.

5. A probe according to any one of the preceding claims, characterised in that the semiconductor laser (1) is mounted at the apex of a conical heat sink (2).

6. The method of effecting biomodulation (stimulation or inhibition) characterised by delivering visible or invisible light energy into a target tissue, nerve or immune system by means of a probe according to any one of the preceding claims.

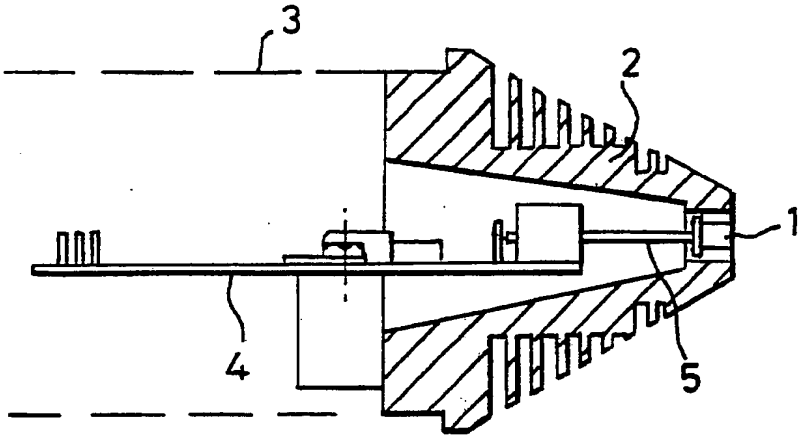


FIG.1.

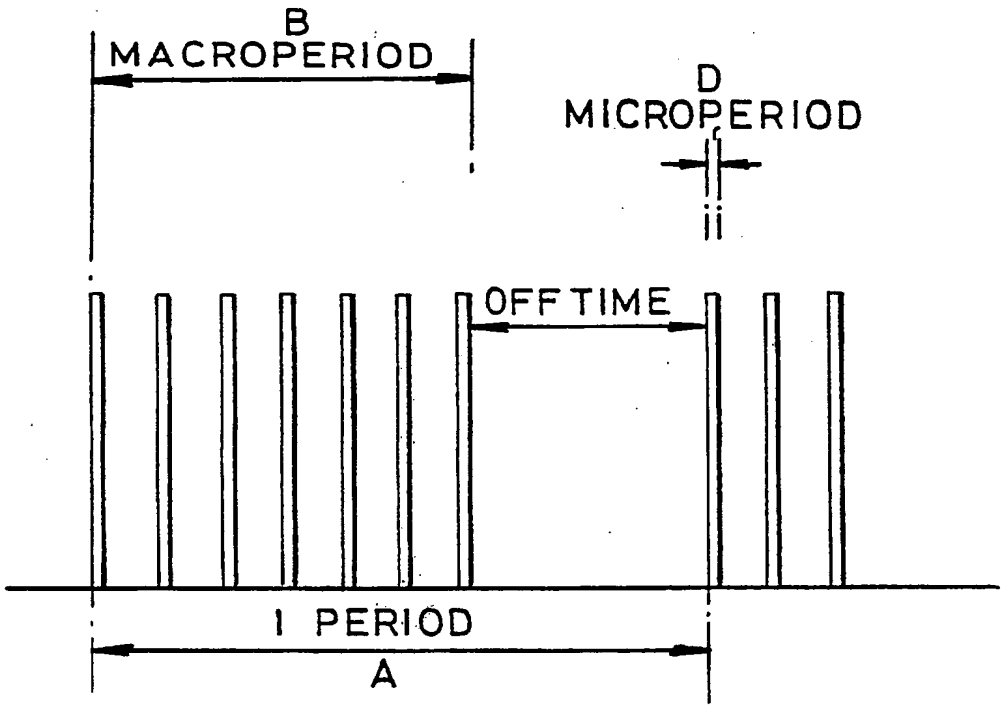
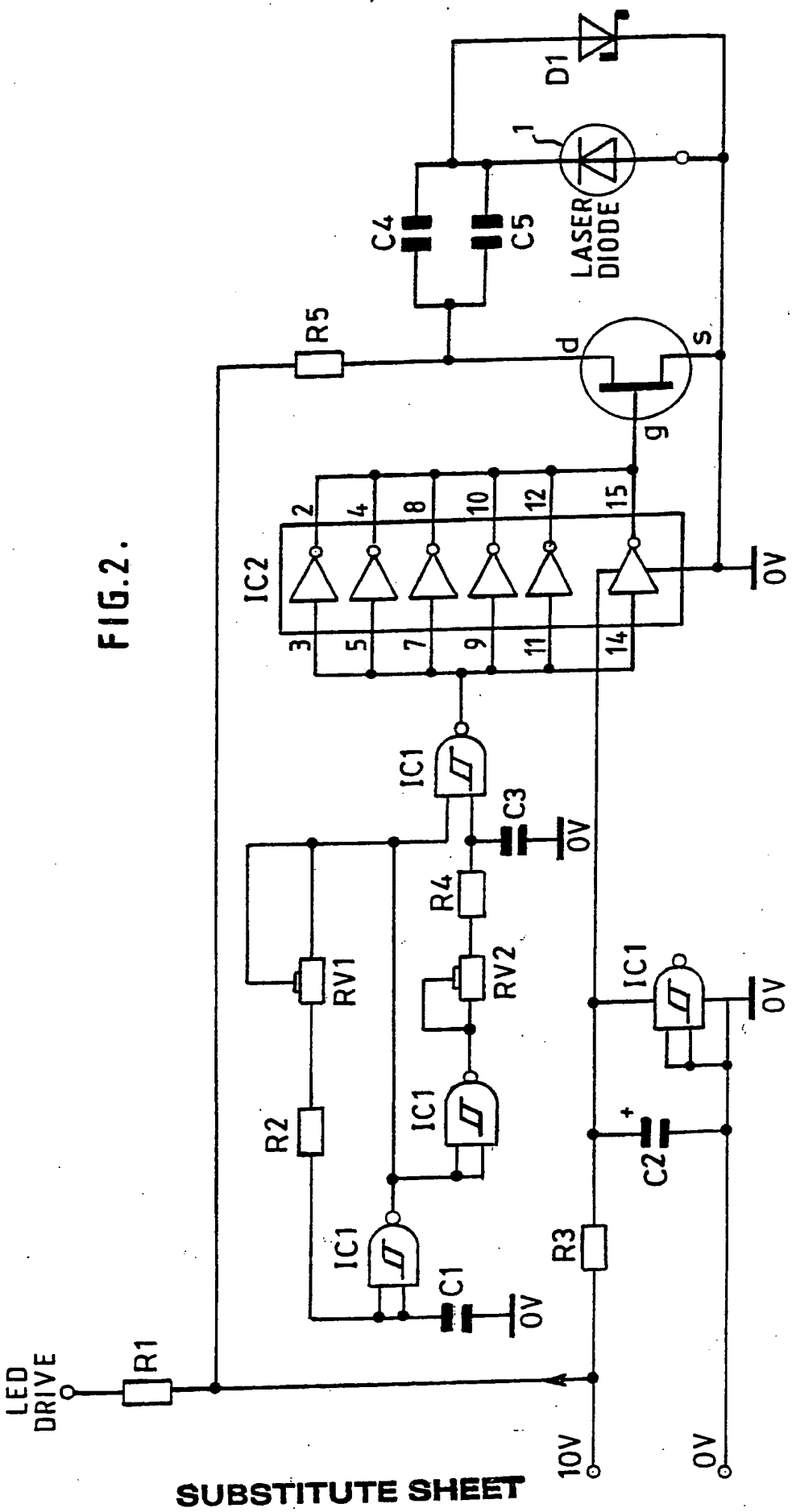


FIG.3.

FIG.2.


D1
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R2
R3
C1
C2
+
LED DRIVE
R1
10V

FURTHER INF RMATION CONTINUED FROM THE SECOND SHEET

V. [X] OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE [1]

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. [X] Claim numbers 6, because they relate to subject matter not required to be searched by this Authority, namely:

See PCT/Rule 39.1(iv): Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.

2. [ ] Claim numbers ....., because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claim numbers ....., because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).

VI. [ ] OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING [2]

This International Searching Authority found multiple inventions in this international application as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.

2. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

3. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:

4. [ ] As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

[ ] The additional search fees were accompanied by applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 91/00197

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC[5]: A 61 N 5/06

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
IPC[5]	A 61 N

Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category *	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
X	FR, A, 2390968 (SKOVAJSA) 15 December 1978 see the whole document	1-4,6
A	---	5
A	DE, A, 3719561 (K.K. MORITA SEISAKUSHO) 21 January 1988 see column 8, lines 28-50	5
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* Special categories of cited documents: [10]

"A" document defining the general state of the art which is not considered to be of particular relevance

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
29th May 1991	-5. 07. 91
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	F.W. HECK

Form PCT/ISA/210 (second sheet) (January 1985)

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. GB 9100197 SA 44861

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 28/06/91 The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
FR-A- 2390968	15-12-78	CA-A- 1133348	12-10-82
		DE-A,C 2820908	23-11-78
		GB-A- 1600217	14-10-81
		JP-C- 1357213	13-01-87
		JP-A- 53145386	18-12-78
		JP-B- 61022587	02-06-86
		NL-A- 7805148	20-11-78
		SE-A- 7805479	17-11-78
		US-A- 4232678	11-11-80
DE-A- 3719561	21-01-88	FR-A- 2599961	18-12-87
		US-A- 4826431	02-05-89